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EXAMINER	
PRIEBE, SCOTT DAVID	

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1632	

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9

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)
	10/032,047	KASPAR ET AL.
	Examiner	**Art Unit**
	Scott D. Priebe	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6,8 .
4) ☐ Interview Summary (PTO-413) Paper No(s)._____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-18 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. Claims 10-18 are directed to a method for increasing proliferation of a nerve cell with a synaptic portion and cell portion, i.e. a neuron (Dorlund's Illustrated Medical Dictionary, p. 1131). Neurons are terminally differentiated cells that are non-dividing, and therefore incapable of proliferating (growing by reproduction of similar cells, Dorlund's Illustrated Medical Dictionary, p. 1361, i.e. undergoing cell division). Neurotrophic factors, such as nerve growth factor and insulin-like growth factor-1, are known to promote survival of neurons, and in some cases to promote neurite outgrowth and axon regeneration *in vitro* and *in vivo* (Yuen et al., Am. Neurol. 40: 346-354, 1996). There is no evidence of record to suggest that treatment of neurons with a growth factor or by transfection of a neuron with a vector encoding a growth factor would overcome nature and induce a neuron to proliferate.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for promoting survival in humans of: a) entorhinal layer II neurons by intrahippocampal injection, or b) nigral-TH positive neurons by intrastriatal injection of a viral vector comprising a gene encoding an anti-apoptotic gene of the Bcl-2 family, or promoting survival of spinal motorneurons by intramuscular injection of a viral vector comprising a gene encoding insulin-like growth factor-1, wherein the genes are expressed, does not reasonably provide enablement for any other embodiments embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 19-27 are broadly directed to a method of treating any unspecified neurodegenerative disease in humans. The method involves introducing a viral vector, such as an AAV vector, comprising an unspecified therapeutic gene, or encoding a member of the Bcl-2 family of anti-apoptotic genes, into the unspecified terminal field of an unspecified target neuron, i.e. introducing the vector into tissue comprising the synaptic end of the target neuron. Retrograde transport of the vector from the synaptic end of the neuron to the cell body (generally located outside the terminal field) is required for transfection. The claims do not require that the therapeutic gene be expressed in the target neuron.

The general subject area of the claimed invention is *in vivo* gene therapy, which at the time the invention was made was highly unpredictable and still largely undeveloped art, despite high skill in the art and extensive experimentation. Orkin et al. reviews the state of the art of gene therapy before the instant invention was made. The overall conclusions were: 1) gene

therapy for each disease would present its own scientific and clinical challenges; 2) no successful gene therapy protocol was known; 3) significant problems remained in all aspects of gene therapy, especially with respect to effective expression vectors; 4) the pathophysiology of diseases to be treated were poorly understood; 5) one cannot predictably extrapolate the result of one animal model, such as mouse, to treatment of a disease in a different animal, such as human; 6) assessment of known gene therapy protocols was hindered by poor gene transfer, reliance on qualitative, rather than quantitative assessments of gene transfer, lack of suitable controls and poor definition of biochemical or disease endpoints; and 7) that gene therapy has been oversold, and the impression that gene therapy is successful is mistaken (pages 1-2). Each of the defects in the gene therapy art as a whole cited by Orkin et al. applies to the instant invention. Verma et al. (Nature 389: 239-242, 1997) reiterates the finding in Orkin that not a single successful gene therapy protocol for humans had been described in the art and that lack of efficient gene delivery and sustained expression remained the Achilles heel of gene therapy (see page 239). The instant specification does not generally correct the deficiencies in the prior art regarding gene therapy. Rather, the specification relies upon the prior art for teaching expression constructs and nucleic acid vectors which have been tried, and some untried, which have not been successful in light of Orkin and Verma. Verma clearly discloses that serious problems existed in this art such that no unequivocal success had been obtained for the treatment of any disease. Verma reports optimism that the problems would be surmounted and that gene therapy would one day be routine, however, there is no evidence of record that it was routine at the time the invention was made, quite the contrary. Rosenberg et al. (Science 287: 1751, 2000) reported that at the time the instant application was filed, there was still no unequivocal instance of clinical efficacy with

gene therapy, and that those in the field were still guilty of overselling gene therapy, despite a decade of failure. Orkin clearly makes the point that gene therapy for each disease would present its own scientific and clinical challenges. Consequently, the specific guidance and working examples provided in the specification for the three specific applications of protecting entorhinal layer II neurons or TH+-dopaminergic neurons with a Bcl-xL gene, and motor neurons with an IGF-1 gene does not provide a basis for extrapolation to other neurodegenerative diseases, or therapeutic genes.

Hsich et al. (Hum. Gene Ther. 13: 579-604, March 2002), published shortly after the instant invention was made, reviews the infant state of gene therapy for human neurologic diseases. It discloses that reasons for the “slow start” to gene therapy for neurologic diseases include the unique difficulties in designing interventions in such a complex organ, the limited access to the brain, and the combination of compartmentalized, discrete functional domains and complex circuitry of the brain (page 579, col. 1). After summarizing what little work has been done in this area, the authors conclude (pages 594-595) by noting that very few gene therapy protocols for peripheral diseases have shown any degree of success, and the daunting task of carrying out gene therapy of the brain. They point out that research in this area is still at the stage of identifying effective means of gene delivery, and toxicity assessment. Also, they warn much as did Orkin, not to let enthusiasm and hope override common sense. The authors express doubt that breakthroughs in this field will arise from the current focus on neuroprotection, and that success will require clear and comprehensive scientific understanding of the pathologic processes and the consequences of the therapeutic genes, and the use of well characterized, safe vectors and delivery modalities. That Hsich raises these concerns at a time after the instant

invention was made, is a clear indication that the requisite knowledge was lacking in the prior art for successful gene therapy of human neurologic disease.

For practice of the method as broadly as claimed, one of skill in the art would be required to know the therapeutic gene(s) to be used for a specific neurodegenerative disease, the target neurons for the that disease, where the terminal filed for that target neuron is to be found, and whether the particular viral vector, such as an AAV vector, would be transported from the synaptic end to the cell body of the target neuron. The specification provides such guidance for protecting a) entorhinal layer II neurons by intrahippocampal injection, or b) nigral-TH positive neurons by intrastriatal injection of an AAV vector comprising a gene encoding an anti-apoptotic gene of the Bcl-2 family, or promoting survival of spinal motorneurons by intramuscular injection of an AAV vector comprising a gene encoding insulin-like growth factor-1, wherein the genes are expressed. However, it fails to provide guidance for other diseases, or for other target neurons. The specification does not provide any working examples of the claimed methods themselves, but does provide working examples in animal models that support enablement of the invention in humans for the three specific applications listed above.

The specification (pages 15-17) discloses that intrahippocampal injection of AAV resulted in substantial retrograde transport of AAV into entorhinal layer II neurons, and possibly hilar neurons and medial septum projection neurons, but at much lower levels. The specification also discloses that intrastriatal injection of AAV resulted in substantial retrograde transport of the AAV only to nigral TH-positive neurons. These results show that retrograde transport of AAV from synaptic regions shows specificity for certain neurons, i.e. not all neurons can be transfected in this manner. The results also show that one cannot predict whether a viral vector,

such as AAV, is capable of transfecting a particular target neuron, i.e. it must be determined empirically. Also, the results in the specification show that any protective effect requires expression of the therapeutic gene, transfection by an AAV vector alone is not sufficient (the claims should be amended to indicate that the therapeutic gene is expressed in the target neuron).

The specification discloses that a variety of neurodegenerative diseases may be treated with the method, including Alzheimer's disease, Parkinson's disease, Multiple Sclerosis, Huntington's disease, Amyotropic Lateral Sclerosis (ALS), Pick's disease, ballism, Guillain-Barre syndrome. However, the specification identifies target neurons for Alzheimer's disease, Parkinson's disease, and ALS, the region of the terminal field of the target neurons, and a therapeutic gene for each. It fails to teach target neurons, the location of their terminal field, or suitable therapeutic genes for any other human neurodegenerative disease. The specification further suggests that therapeutic genes may be employed such as encoding antisense to unspecified glutamate receptors, FGF, NT-3, BDNF and GDNF. However, the specification fails to identify one or more of the target disease, target neuron, or the location of the terminal field of the target neuron where these therapeutic genes would be used. There is no prior art of record disclosing successful treatment of a neurodegenerative disease in a human, much less a treatment involving administration of the vector to the terminal field of the target neurons. The prior art of record discloses examples in animal model systems where expression of certain therapeutic genes appeared to provide some beneficial effect. However, most of these instances involved injection of the viral vectors to the location of the cell bodies of the target neurons, not to their terminal fields. In some cases, retrograde or anterograde transport of the gene product and vector

was examined, but generally was limited to transport of the gene product rather than the vector, see for example Ozawa et al., US 2003/0050273, para. 0165.

With respect to the choice of transgene, Simon et al. (Human Gene Therapy 10: 1715-1720, 1999) disclose that contrary to expectation, transfection of retinal ganglion cells with an AAV vector carrying a bcl-2 gene led to a greater susceptibility to apoptosis in response to exitotoxic stimuli. This finding illustrates that while bcl-2 may protect some neurons from apoptosis, a protective effect of bcl-2 therapy cannot be predicted for all neurons. Finiels et al. (US 6,632,427 B1) disclosed that intramuscular injection of an adenoviral vector expressing NT-3 extended the life-span of SOD* transgenic mice, an animal model for ALS. The adenoviral vector transfected motor neurons via retrograde transport to the cell bodies in the spine. However, treatment with adenoviral vectors expressing GDNF, CTNF, BDNF, or combinations thereof, had no effect on survival. These findings illustrate that the protective effect of specific neurotrophic factors on specific neurons is not predictable, empirical testing is required to determine which neurotrophic factor will protect a given neuron.

It has long been recognized in the chemical and biological arts that the unpredictability of a particular art area may alone provide a reasonable doubt as to the accuracy of a broad statement made in support of the enablement of a claim. *Ex parte Singh*, 17 USPQ2d 1714, 1715 (BPAI 1991), *In re Marzocchi*, 169 USPQ 367, 369-370 (CCPA 1971). As set forth in *In re Fisher,* 166 USPQ 18, 24 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and

> physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

The specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. The rule that a specification need not disclose that which is well known in the art simply means that omission of minor details does not cause a specification to fail the enablement requirement, and is not a substitute for an enabling disclosure. However, if there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings cannot be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). The specification is silent with regard to guidance critical to carrying out the invention as broadly as it is claimed, such as identifying target neurons, administration sites, and therapeutic genes for treating the range of neurodegenerative diseases. In this case, the prior art is of little or no help at all since those in the art had been unsuccessful in achieving any unequivocal instance of effective treatment with gene therapy in humans. Consequently, due to the high unpredictability in the

relevant art and the lack of specific guidance and working examples for the breadth of embodiments embraced by the claims, undue experimentation would be required to carry out the invention as broadly as it is claimed.

Claims 12 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 12, claim 10 recites the step of "incubating said nerve cell under conditions …". The term incubate (or incubation) in the context of a cell means to maintain the cells in a medium under controlled environmental conditions, i.e. cell culture. The specification describes transfection of nerve cells (neurons) *in vivo*, and does not explicitly describe transfection of nerve cells in culture. Claim 12 explicitly recites that the method is carried out *in vivo,* consistent with the description, i.e. in an animal having nerve cells, but inconsistent with recitation of the term "incubating" in claim 10. It is unclear what the step of "incubating" entails in the context of transfecting neurons *in vivo.*

Claim 17 recites "a nerve growth factor". Claim 18 recites "wherein said nerve growth factor is insulin-like growth factor-1 (IGF-1). As disclosed in Koliatos (Crit. Rev. Neurobiol. 10: 205-238, 1996, at pages 213-214) and Yuen (Am. Neurol. 40: 346-354, 1996, Table 1), nerve growth factor or NGF, is a specific trophic factor of the NGF or neurotrophin family, which includes NGF and structurally related trophic factors such as BDNF, NT-3, and NT-4/5. This family does not include IGF-1. The specification mentions nerve growth factor only once (p. 22, para. 0047, line 2) as an alternative to IGF-1, not as embracing IGF-1. Consequently, it is unclear

what the term "nerve growth factor" in claim 17 means and what the metes and bounds of claim 17 are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 8, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Senut et al (J. Neurosci. 20: 219-229, Jan. 2000).

Senut discloses injection of 3 x 10^6 infectious particles of AAV-GFP or AAV-97Q-GFP into the striatum of rats (page 220). GFP expression was observed after 6 months (Fig. 8). Expression of the gene products was observed in the substantia nigra and ventral tegmental area, consistent with retrograde transport of the vectors from the injection, although the authors could not distinguish between transport of the gene product or of the vector site (pages 224 & 226, col. 2). The specification (pp. 15-16, para. 0025) discloses that injection of AAV-GFP into the striatum transduces neurons whose synaptic portion lies in the striatum and whose cell body lies in the substantia nigra pars compacta via retrograde transport of the vector. Absent evidence to the contrary, it is presumed that the retrograde transport observed by Senut included transport of the vector.

Claims 1-4, 8 and 9 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Peterson et al. (European Journal of Neuroscience 12 (Suppl. 11): 233, Abstract 110.13, June 2000).

Peterson discloses injection of AAV vectors expressing a GFP/Bcl-xL fusion protein or GFP into the hippocampus (dentate gyrus), resulting in transfection of hippocampal neurons and transfection of entorhinal class II neurons (ECL2 neurons) projecting into the dentate gyrus by retrograde transport. Expression of the GFP/Bcl-xL fusion protein protected the ECL2 neurons from loss due to a subsequent perforant pathway lesion. Peterson further teaches that AAV vectors can be used to deliver therapeutic transgenes in animal models of Alzheimer's disease.

Claims are 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bartlett et al. (Hum. Gene Ther. 9: 1181-1186, 1998), as evidenced by Xiao et al. (Exp. Neurol. 144: 113-124, 1997) and the instant specification at pages 13-16.

Bartlett discloses a method of transfecting neurons in rats with an AAV vector expressing GFP by intrahippocampal injection of 2.5×10^{10} vector particles (1 μl of vector at 2.5×10^{13} particles/ml). As disclosed by Xiao (page 115, col. 1), this dose should be approximately equivalent to 2.5×10^{8} infectious particles. Bartlett does not disclose that retrograde transport of the vector had occurred, nor is it apparent that it had been looked for. However, this experiment is essentially the same as disclosed in the instant specification at page 13-16. Consequently, retrograde transport of the vector and extended expression of GFP must have inherently occurred in these rats, i.e. since the method was the same, the results should be the same.

Claims 1, 2, 4-7, 19, 20, 22-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Horellou et al., US 2002/0031493 A1.

Horellou et al. discloses a method of treating Parkinson's disease by intrastriatal injection of an adenoviral vector comprising a therapeutic gene encoding GDNF. In a rat model system (the same as described in the instant specification), 1.5 x 10^8 pfu were injected into each rat. Neurons of both the striatum and substantia nigra were transfected. In the latter, transfection occurred via retrograde transport. Expression of GDNF protected the striatal and nigral neurons from death. It is evident that for treating humans, a substantially higher dose of vector would be required. See entire document, especially Example 4. Since the GDNF protects the neurons from apoptosis, it meets the limitation as being the product of an anti-apoptotic gene, as broadly interpreted.

Claims 1, 2, 4-7, 19, 20, 22-24 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Finiels et al., US 6,632,427 B1.

Finiels discloses a method for treating ALS by intramuscular injection of an adenoviral vector expressing NT-3. Motor neurons are transfected via retrograde transport form the muscle. In SOD* mice, a model system for severe ALS, 5-10 x 10^9 pfu were injected, and the treatment extended the life span of the mice. It is evident that for treating humans, a substantially higher dose of vector would be required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-21 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (European Journal of Neuroscience 12 (Suppl. 11): 233, Abstract 110.13, June 2000).

Peterson discloses injection of AAV vectors expressing a GFP/Bcl-xL fusion protein or GFP into the hippocampus (dentate gyrus), resulting in transfection of hippocampal neurons and transfection of entorhinal class II neurons (ECL2 neurons) projecting into the dentate gyrus by retrograde transport. Expression of the GFP/Bcl-xL fusion protein protected the ECL2 neurons from loss due to a subsequent perforant pathway lesion. Peterson further teaches that AAV vectors can be used to deliver therapeutic transgenes in animal models of Alzheimer's disease, which indicates that the perforant pathway lesion in the rat is a model for Alzheimer's disease.

Peterson does not explicitly teach using the disclosed method to treat Alzheimer's disease in humans. However, since the rat used is a model for deterioration of entorhinal neurons in human Alzheimer's patients at early stages of the disease, the results disclosed provide evidence for a reasonable expectation of success for protecting entorhinal neurons from degeneration in human Alzheimer's patients. It would therefore have been *prima facie* obvious to one of skill in the art at the time the instant invention was made to have practiced Peterson's method on human Alzheimer's patients.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 19-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application No. 10/237,567. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-9 embrace the subject matter of claimed in the '567 application. Also, instant claims 19-27 embrace subject matter also embraced by the claims of the '567 application. The claims of the '567 application are limited to delivery

of the viral vector to muscle tissue to transfect neurons whose cell bodies lie elsewhere, but are not limited to humans; whereas instant claims 19-27 are not limited to any particular class of neuron or neurodegenerative disease, but are limited to humans. When the claims of '567 are read in light of its specification, human subjects are explicitly disclosed as being targets of the method claimed. These embodiments are embraced by the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

Scott D. Priebe
Primary Examiner
Art Unit 1632